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EXAMINER	
EMCH, GREGORY S	
ART UNIT	**PAPER NUMBER**
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/544,093	YEDNOCK ET AL.	
	Examiner	Art Unit	
	Gregory S. Emch	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 November 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *103-140* is/are pending in the application.

4a) Of the above claim(s) *128-131,139 and 140* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *103-127 and 132-138* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *08/01/05, 03/09/05, 10/06/08, 10/08/08, 11/17/08*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☒ Other: *Sequence alignments A-C*.

DETAILED ACTION

Response to amendment

Claims 1, 6, 8, 26, 28, 32, 48, 53, 55, 73, 75, 79 and 95 have been canceled and new claims 103-140 have been added in the amendment filed on 17 November 2008. Following the amendment, claims 103-140 are pending in the instant application.

Election/Restrictions

Applicants' election without traverse of Group II, claim 95, in the reply filed on 17 November 2008 is acknowledged. Applicants assert that newly submitted claims 103-138 read on the elected invention.

Claims 139 and 140 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 17 November 2008.

Regarding newly submitted claims 128-131, said claims are directed to an invention that is independent or distinct from the elected invention for the following reasons: Applicants have elected Group II, which encompasses subject matter recited by now canceled claim 95. As set forth in the restriction requirement of 16 June 2008, Group II and claim 95 encompass a pharmaceutical composition comprising a fragment of Aβ, wherein the fragment induces antibodies that specifically bind to Aβ at one or more epitopes between residues 12 and 43 without inducing antibodies that specifically

bind to one or more epitopes between residues 1-11, wherein the fragment is not Aβ13-28, 17-28, 25-35, 35-40, 33-42 or 35-42. Thus, fragments of Aβ, which induce antibodies that specifically bind to one or more epitopes of between residues 1-11 (as embraced by claims 128-131) are considered non-elected subject matter. Accordingly, claims 128-131 are withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03. It is noted that claims 114-117 have not been withdrawn because said claims are directed to a product and the intended use of the product, and the intended use has not been given patentable weight.

Claims 103-127 and 132-138 are under examination in the instant office action.

Information Disclosure Statement

Signed and initialed copies of the IDS papers filed on 01 August 2005, 09 March 2008, 06 October 2008, 08 October 2008 and 17 November 2008 are enclosed in this action.

Claim Objections

Claims 103 is objected to because of the following informalities: the claim does not define the acronym Aβ at its first mention. It is suggested that "amyloid-β" is added before Aβ in line 1 of the claim.

Claims 104-113 are objected to because of the following informalities: The claims depend from independent claim 103, which is directed to a fragment of Aβ

consisting of the amino acid sequence KLVFFAED (residues 16-23 of SEQ ID NO: 1). Because of the "consisting of" closed language recited by claim 103, dependent claims 104-113 improperly broaden the claimed fragment by reciting additional elements that should be excluded by the closed language of independent claim 103.

Appropriate correction is required.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 103 and 114-117 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

Claim 103 is directed to a fragment of Aβ consisting of the amino acid sequence KLVFFAED (residues 16-23 of SEQ ID NO: 1). Claims 114-117 are directed to said fragment of Aβ, wherein the fragment is administered in a regime with an N-terminal Aβ fragment (claim 114), wherein the N-terminal Aβ fragment is Aβ1-5 (claim 115), Aβ1-6 (claim 116) and Aβ1-7(claim 117). The limitations of "wherein the fragment is administered…" in claims 114-117 do not describe added limitations of the product itself. Rather, said limitations are analogous to the intended use of the product and do not result in a structural difference in the claimed invention (claim 103 vs. claims 114-117).

Thus, the claims, as written, do not sufficiently distinguish the claimed invention over proteins that exist naturally because the claims do not particularly point out any non-naturally occurring differences between the claimed products and the naturally occurring products. It appears that the claimed peptide (residues 16-23 of Aβ) exists in nature (see rejection under 35 U.S.C. 102(b), below). In the absence of the hand of man, the naturally occurring product is considered non-statutory subject matter. *See Diamond v. Chakrabarty*, 447 U.S. 303, 206 USPQ 193 (1980). The claims should be amended to indicate the hand of the inventor by insertion of "isolated" or "purified," for example. See MPEP 2105.

Claim Rejections - 35 USC § 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 114-117 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claims are directed to a fragment of Aβ consisting of the amino acid sequence KLVFFAED (residues 16-23 of SEQ ID NO: 1), wherein the fragment is administered in a regime with an N-terminal Aβ fragment (claim 114), wherein the N-terminal Aβ fragment is Aβ1-5 (claim 115), wherein the N-terminal Aβ fragment is Aβ1-6 (claim 116) and wherein the N-terminal Aβ fragment is Aβ1-7(claim 117).

MPEP § 2173.05(p) states that a single claim which claims both an apparatus and the method steps of using the apparatus is indefinite under 35 U.S.C. 112, second paragraph. **IPXL Holdings v. Amazon.com, Inc.*, 430 F.2d 1377, 1384, 77 USPQ2d 1140, 1145 (Fed. Cir. 2005); *Ex parte Lyell*, 17 USPQ2d 1548 (Bd. Pat. App. & Inter. 1990) *(claim directed to an automatic transmission workstand and the method * of using it * held ** ambiguous and properly rejected under 35 U.S.C. 112, second paragraph). Therefore, since the instant claims encompass a product and process of using the product in each of the claims, the claims are indefinite.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 103 and 114-117 are rejected under 35 U.S.C. 102(b) as being anticipated by WO9639834-A1 to Soto-Jara et al.

Claim 103 is directed to a fragment of Aβ consisting of the amino acid sequence KLVFFAED (residues 16-23 of SEQ ID NO: 1). Claims 114-117 are directed to said fragment of Aβ, wherein the fragment is administered in a regime with an N-terminal Aβ fragment (claim 114), wherein the N-terminal Aβ fragment is Aβ1-5 (claim 115), Aβ1-6 (claim 116) and Aβ1-7(claim 117).

WO9639834-A1 to Soto-Jara et al. teaches a fragment of Aβ consisting of the residues 16-23 of SEQ ID NO: 1 (see attached Sequence alignment A, SEQ ID NO: 1 of

the WO document at pp. 34-35, and Figure 1A of the WO document). The WO document refers to this peptide as "amyloid β-peptide," states that it is an amyloidogenic sequence responsible for amyloid deposits in patients with Alzheimer's disease and that this peptide has a high probability of adopting a β-sheet structure (p.9, lines 14-35 and Figures 1A-B). Claims 114-117 are anticipated by the WO document because the limitations of "wherein the fragment is administered…" in these claims do not describe added limitations of the product itself. Rather, said limitations are analogous to the intended use of the product and do not result in a structural difference between the claimed invention and the prior art. A recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the limitations of the claim. Thus, to meet the limitations of the claimed product in claims 114-117, a prior art reference need only teach a fragment of Aβ consisting of the residues 16-23 of SEQ ID NO: 1, which the WO document teaches. Since the reference teaches all the required elements of the claimed product, claims 103 and 114-117 are anticipated by WO9639834-A1 to Soto-Jara et al.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the

> invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 103-109, 112-124, 127, 132-135, 137 and 138 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 96/39834 A1 to Soto-Jara et al., in view of WO 99/27944 A1 to Schenk (citation 58 on IDS dated 01 August 2005).

WO 96/39834 A1 to Soto-Jara et al. teaches as set forth above, including the relevant disclosure of the limitations of claims 103 and 114-117. The difference between the disclosure of the Soto-Jara et al. document and the claimed invention is

that the reference does not teach the fragment of Aβ conjugated to a carrier or as part of a pharmaceutical composition.

However, upon reading the disclosure of the '834 document, the skilled artisan would have recognized the desirability of developing improved compositions for treating Alzheimer's disease. Furthermore, WO 99/27944 A1 to Schenk teaches methods of treatment of a disease characterized by amyloid deposition by inducing an immune response against a peptide component of an amyloid deposit. The methods are practiced via administration of Aβ peptide, i.e. amyloid β-peptide or an active fragment thereof, to induce the immune response (i.e. to promote the production of Aβ antibodies through active immunization) (p.3, line 1 – p.4, line 30). The Schenk document teaches pharmaceutical compositions for use in these methods, which comprise both the Aβ peptide or fragment and a pharmaceutically acceptable carrier, including compositions that comprise an adjuvant that enhances the immune response to the peptide or fragment (p.3, lines 18-27 and p.4, lines 23-30), as in claims 113, 118, 119 and 132. The Schenk document teaches that the adjuvant can be: alum (p.3, line 23 and p.4, line 30) as in claim 133, MPL (p.3, lines 23-24) as in claim 134, or QS-21 (p.27, line 6), as in claim 135. It is taught that the Aβ fragment can be linked to a carrier molecule, including a heterologous polypeptide (p.19, line 33 – p.20, line 37), as in claims 104, 109 and 124. Also, multiple copies of the fragment can be linked to a single carrier molecule (p.20, lines 36-37), as in claims 105 and 120. The fragment can be linked to the carrier through chemical crosslinking, as in claim 108 and 123, and wherein spacers are present (p.20, lines 13-32) as in claims 107 and 122. It is taught that the carrier can

be diphtheria toxoid (p.5, lines 3-5), as in claims 112 and 127. The pharmaceutical composition comprising the Aβ fragment and adjuvant can be included in a vial (p.27, lines 15-16), as in claim 138. The pharmaceutical compositions can comprise a surfactant (p.28, line 34), as in claim 137.

As evidenced by the prior art, the skilled artisan would have known that residues 16-23 of Aβ are implicated in the neuropathology of amyloid fibril formation. This is because the Soto-Jara et al. document refers to the peptide of residues 16-23 as "amyloid β-peptide," states that it is an amyloidogenic peptide responsible for amyloid deposits in patients with Alzheimer's disease and that this peptide has a high probability of adopting a β-sheet structure (p.9, lines 14-20). Furthermore, it would have been reasonable to predict that a peptide consisting of residues 16-23 of Aβ could be successfully used as part of an immunizing composition useful in methods of treating Alzheimer's disease for several reasons. As set forth above, the Schenk document teaches that the active immunization methods comprise administration of "Aβ peptide," i.e. amyloid β-peptide (p.3, line 1 – p.4, line 30) and the Soto-Jara et al. document refers to the peptide of residues 16-23 of Aβ as "amyloid β-peptide." Thus, it would be prima facie obvious to use the "amyloid β-peptide" of Soto-Jara et al. as the "Aβ peptide" disclosed by Schenk. Moreover, at p. 15, lines 5-10, Schenk teaches fragments as short as 5, 6, or 10 amino acids are immunogenic and that residues 13-28 and 17-28 each are immunogenic. Given that Schenk teaches raising antibodies against the Aβ peptide or active fragments by administering the peptides or active fragments, and given that Soto-Jara et al. teach that a peptide of residues 16-23 of Aβ is a fibril-forming

or β-sheet forming peptide responsible for the pathology of Alzheimer's disease, the skilled artisan would have found it obvious to administer this particular fragment in order to raise antibodies against it and thereby inhibit fibril formation. Therefore, it would have been obvious to the person of ordinary skill in the art at the time the invention was made to provide the amyloidogenic Aβ peptide taught by the Soto-Jara et al. document in a pharmaceutical composition as taught by Schenk to yield predictable results. This is because the artisan has good reason to pursue the known options within his or her technical grasp to obtain predictable results. Such would amount to substitution of known equivalent elements, i.e. one Aβ peptide for another, to yield predictable results.

Regarding claims 106 and 121, neither of the references explicitly teaches a composition comprising the Aβ fragment, wherein a single copy of the fragment is linked to multiple copies of the carrier. However, the Schenk document does teach providing a single copy of the fragment with multiple carriers, i.e. adjuvants (p.27, line 30). Thus, in the instant case, providing a single copy of the fragment with multiple copies of the carrier is clearly a result effective parameter that a person of ordinary skill in the art would routinely optimize (see MPEP §2144.05). Optimization of parameters is a routine practice that would be obvious for a person of ordinary skill in the art to employ. It would have been customary for an artisan of ordinary skill to determine the optimal Aβ composition by varying the number of copies of the carrier to best achieve the desired results. Thus, absent some demonstration of unexpected results from the claimed parameters, this optimization would have been obvious at the time of applicants' invention.

Claims 110, 111, 125 and 126 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 96/39834 A1 to Soto-Jara et al. in view of WO 99/27944 A1 to Schenk (citation 58 on IDS dated 01 August 2005), and further in view of WO 00/72876 A2 to Schenk (citation 323 on IDS dated 01 August 2005).

WO 96/39834 A1 to Soto-Jara et al. and WO 99/27944 A1 to Schenk teach as set forth above. Although the '944 document to Schenk discloses that tetanus toxoid may be used as a carrier (p.20, line 5), the reference does not disclose the tetanus toxoid T cell epitope of the instant SEQ ID NO: 8, nor does it disclose the T cell epitope of the instant SEQ ID NO: 11.

However, upon reading the disclosures of the '834 and '944 documents, the skilled artisan would have recognized the desirability of developing improved compositions for treating Alzheimer's disease. Furthermore, WO 00/72876 A2 to Schenk teaches that preferred carriers for use in Aβ immunizing compositions are the T cell epitopes that comprise the instant SEQ ID NO: 8 or SEQ ID NO: 11 (see attached Sequence alignments B and C, and p.43, lines 14 and 19 of the '876 document), as in claims 110, 111, 125 and 126.

As evidenced by the prior art, the skilled artisan would have known that T cell epitopes that comprise the instant SEQ ID NO: 8 or the instant SEQ ID NO: 11 would be useful as carriers in Aβ immunizing compositions. Furthermore, it would have been reasonable to predict that such T cell epitopes could be successfully used as carriers in the immunizing composition. Therefore, it would have been obvious to the person of

ordinary skill in the art at the time the invention was made to provide the amyloidogenic Aβ peptide taught by the Soto-Jara et al. reference in a pharmaceutical composition(s) as taught by both Schenk documents to yield predictable results. This is because the artisan has good reason to pursue the known options within his or her technical grasp to obtain predictable results. Such would amount to substitution of known equivalent elements, i.e. one carrier for another, to yield predictable results.

Claim 136 is rejected under 35 U.S.C. 103(a) as being unpatentable over WO 96/39834 A1 to Soto-Jara et al. in view of WO 99/27944 A1 to Schenk (citation 58 on IDS dated 01 August 2005), and further in view of WO 01/78777 A2 to Mossman et al.

WO 96/39834 A1 to Soto-Jara et al. and WO 99/27944 A1 to Schenk teach as set forth above, but fail to teach the adjuvant RC-529.

However, upon reading the disclosures of the '834 and '944 documents, the skilled artisan would have recognized the desirability of developing improved compositions for treating Alzheimer's disease. Furthermore, WO 01/78777 A2 to Mossman et al. teaches that a preferred adjuvant is RC-529 (e.g. abstract), as in claim 136.

As evidenced by the prior art, the skilled artisan would have known that RC-529 would be useful as an adjuvant in Aβ immunizing compositions. Furthermore, it would have been reasonable to predict that such an adjuvant could be successfully included in the immunizing composition. Therefore, it would have been obvious to the person of ordinary skill in the art at the time the invention was made to provide the amyloidogenic

Aβ peptide taught by the Soto-Jara et al. reference in a pharmaceutical composition(s) as taught by Schenk and Mossman et al. to yield predictable results. This is because the artisan has good reason to pursue the known options within his or her technical grasp to obtain predictable results. Such would amount to substitution of known equivalent elements, i.e. one adjuvant for another, to yield predictable results.

Conclusion

No claims are allowed.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gregory S. Emch whose telephone number is (571) 272-8149. The examiner can normally be reached 9:00 am - 5:30 pm EST (M-F).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey J. Stucker can be reached at (571) 272-0911. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/G.E./

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02 February 2009

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